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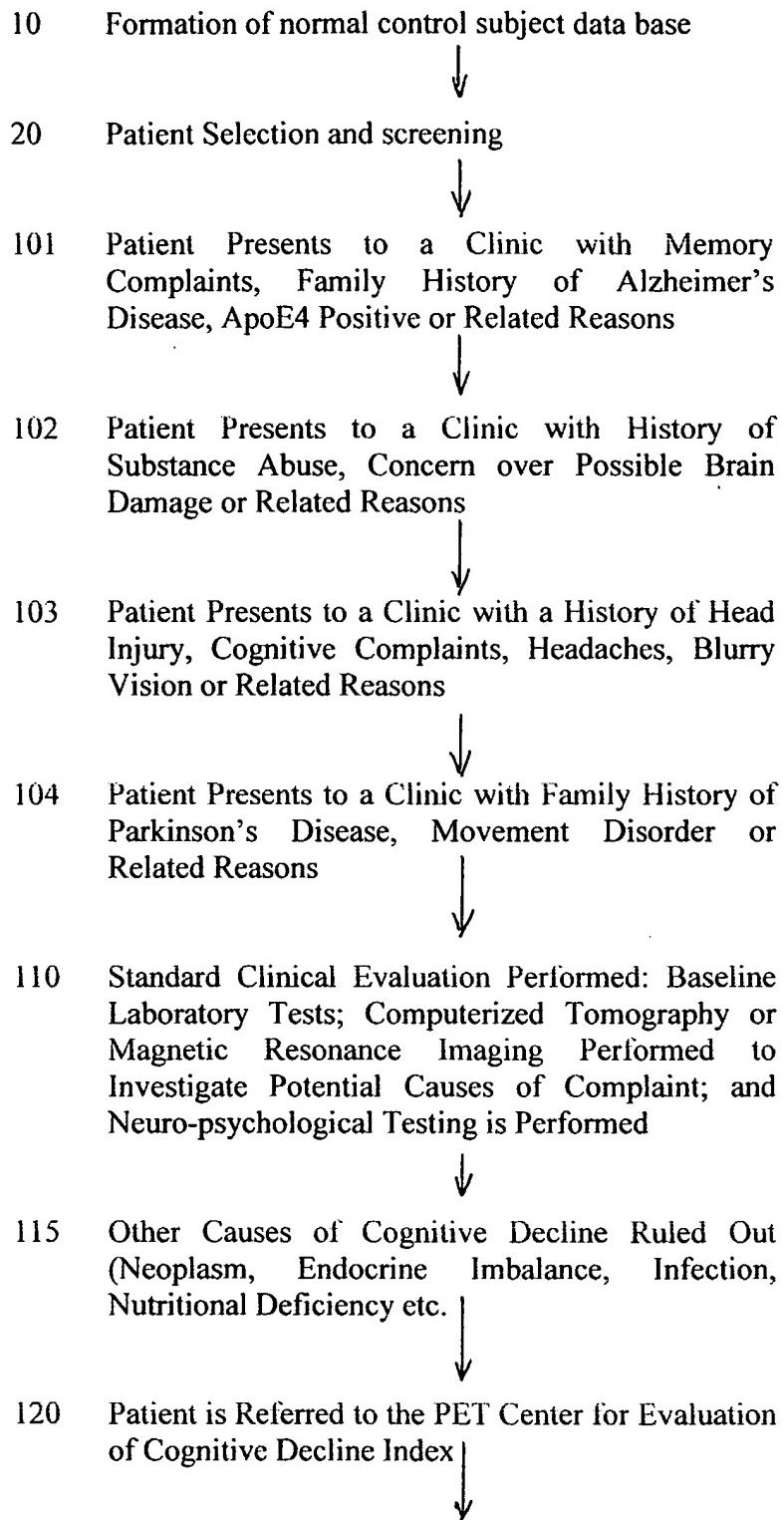
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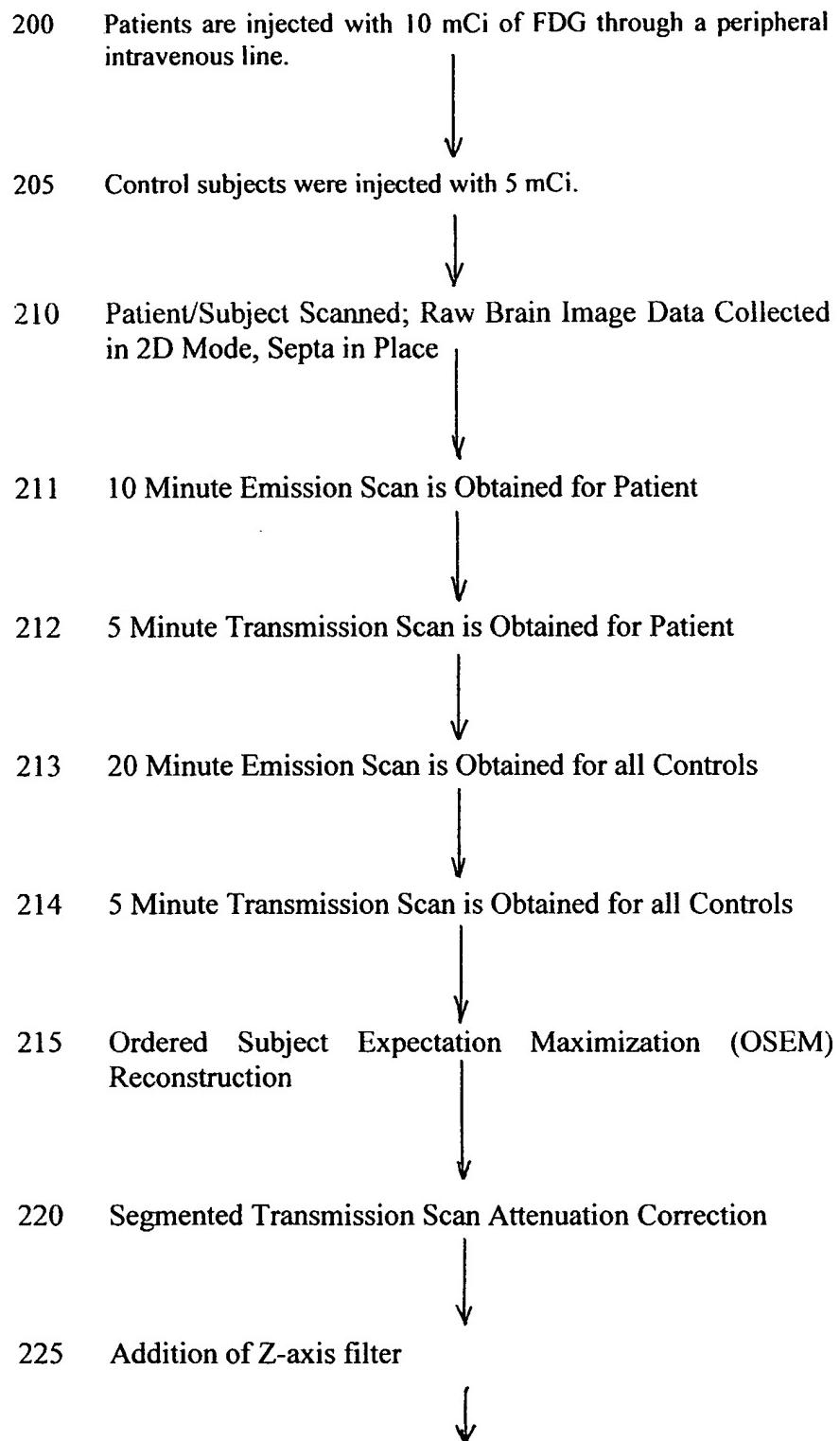
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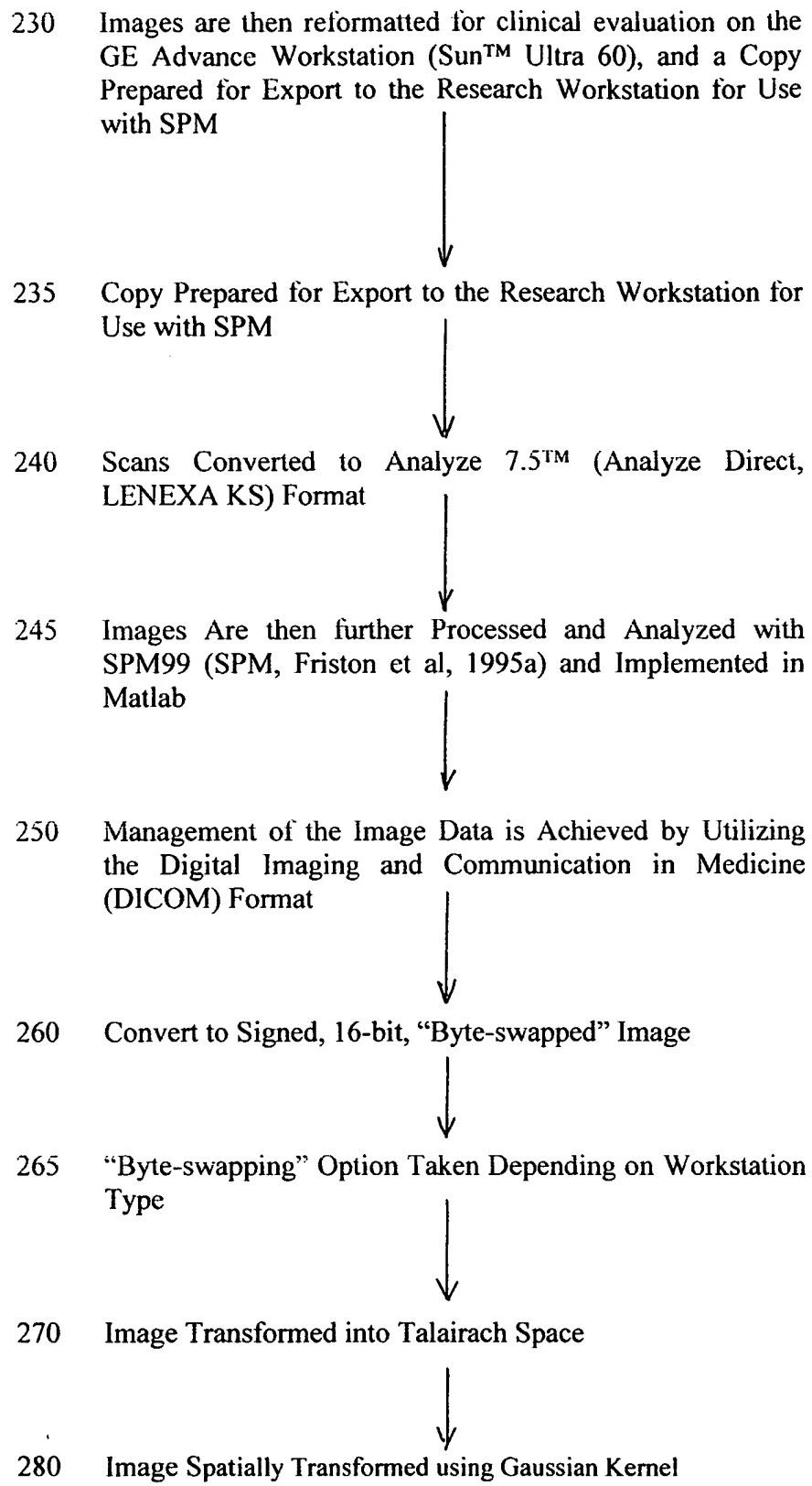
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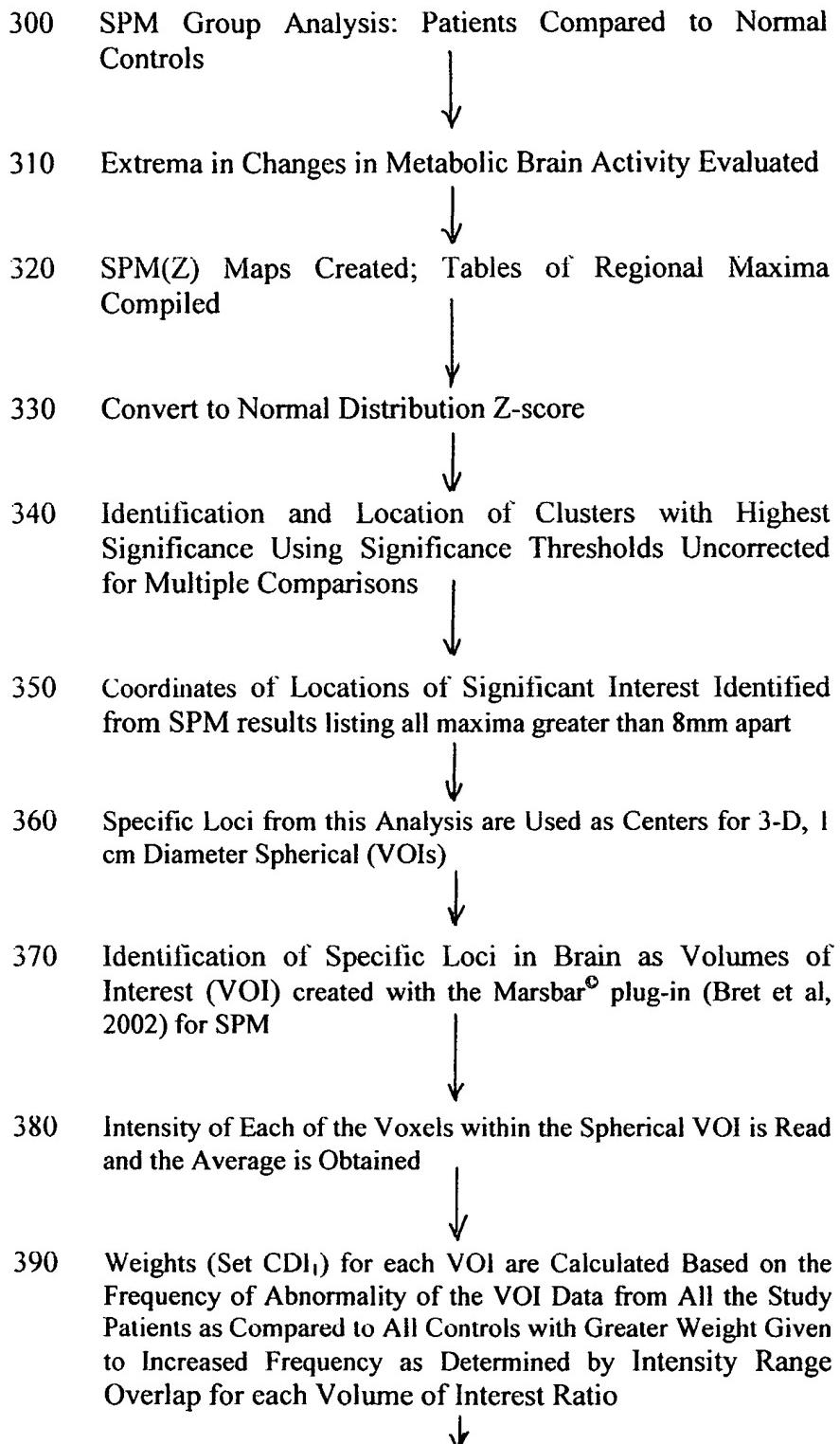
**FIG. 1 Normal Subject Controls and Patient Selection for Development of the Cognitive Decline Index**



**FIG. 2a Derivation of the Processed Digital Brain Image**



**FIG. 2a (Cont'd) Derivation of the Processed Digital Brain Image**



**FIG. 2b Derivation of Region Location and Identification of VOIs**

- 391 Import VOI Data Into Spreadsheet
- 392 Determine Intensity Range Overlap for each VOI Ratio
- 393 Create Weights for each Intensity Extreme
- 394 Create Weighted VOI Ratio
- 395 Scale and Normalize Ratio
- 400 Calculation of CDI:

$$CDI = C_x + \left[ \sum_{j=1}^n V_j X_j / n \right] / \left[ \sum_{i=1}^m W_i Y_i / m \right]$$

Where  $X_j$  denotes the  $j^{\text{th}}$  Increased Intensity Value;  
 $V_j$  denotes the  $j^{\text{th}}$  Weight for the  $j^{\text{th}}$  Increased Intensity Value;  
 $Y_i$  denotes the  $i^{\text{th}}$  Decreased Intensity Value; and  
 $W_i$  denotes the  $i^{\text{th}}$  Weight for the  $i^{\text{th}}$  Decreased Intensity Value.

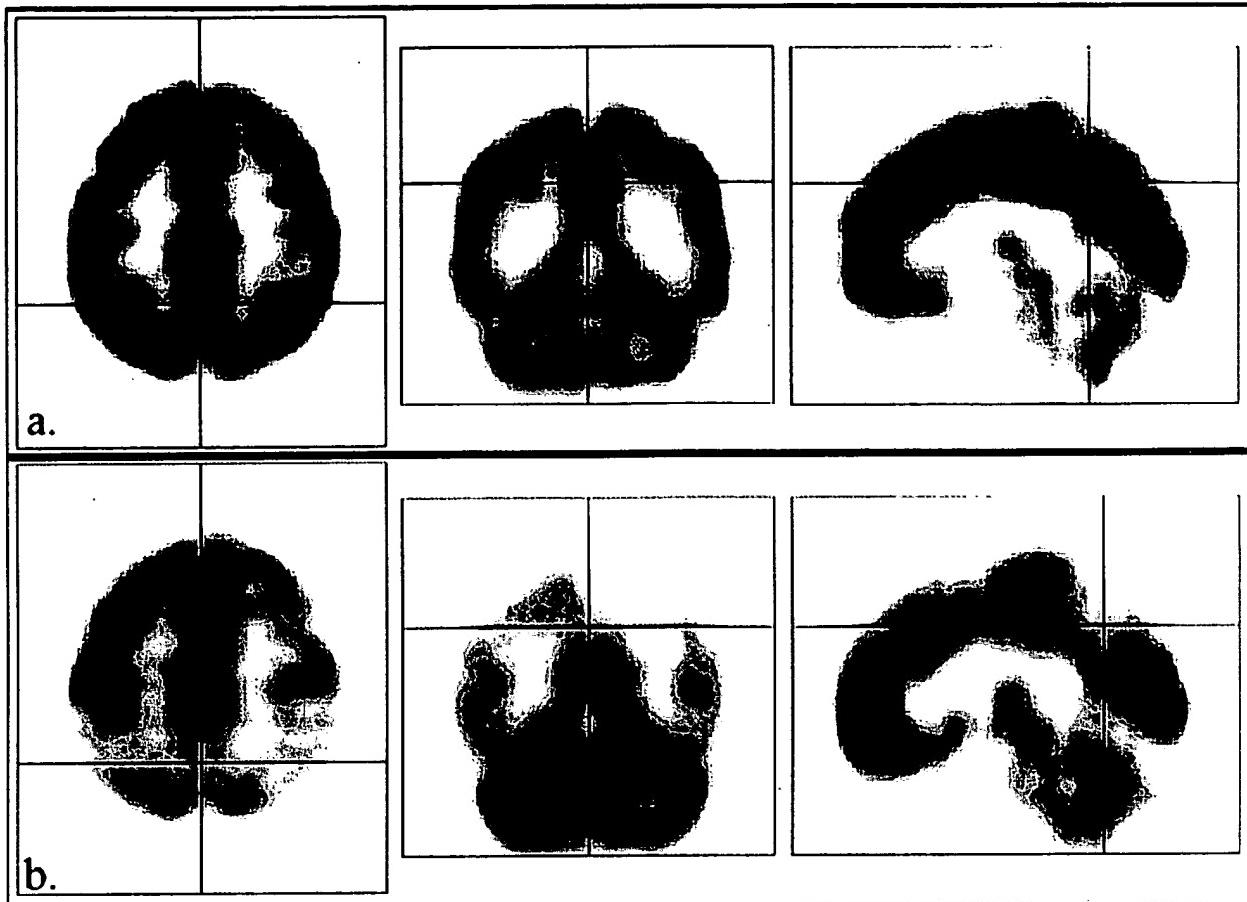
$C_x$  is the correction factor used to normalize the dataset.

- 410 Weights of Set  $CDI_1$  are then used as a baseline for calculation of a second set of Weights (Set  $CDI_2$ ) to calculate  $CDI_2$ . Set  $CDI_2$  is calculated by iterative optimization of each weight to maximally separate the patient from the controls

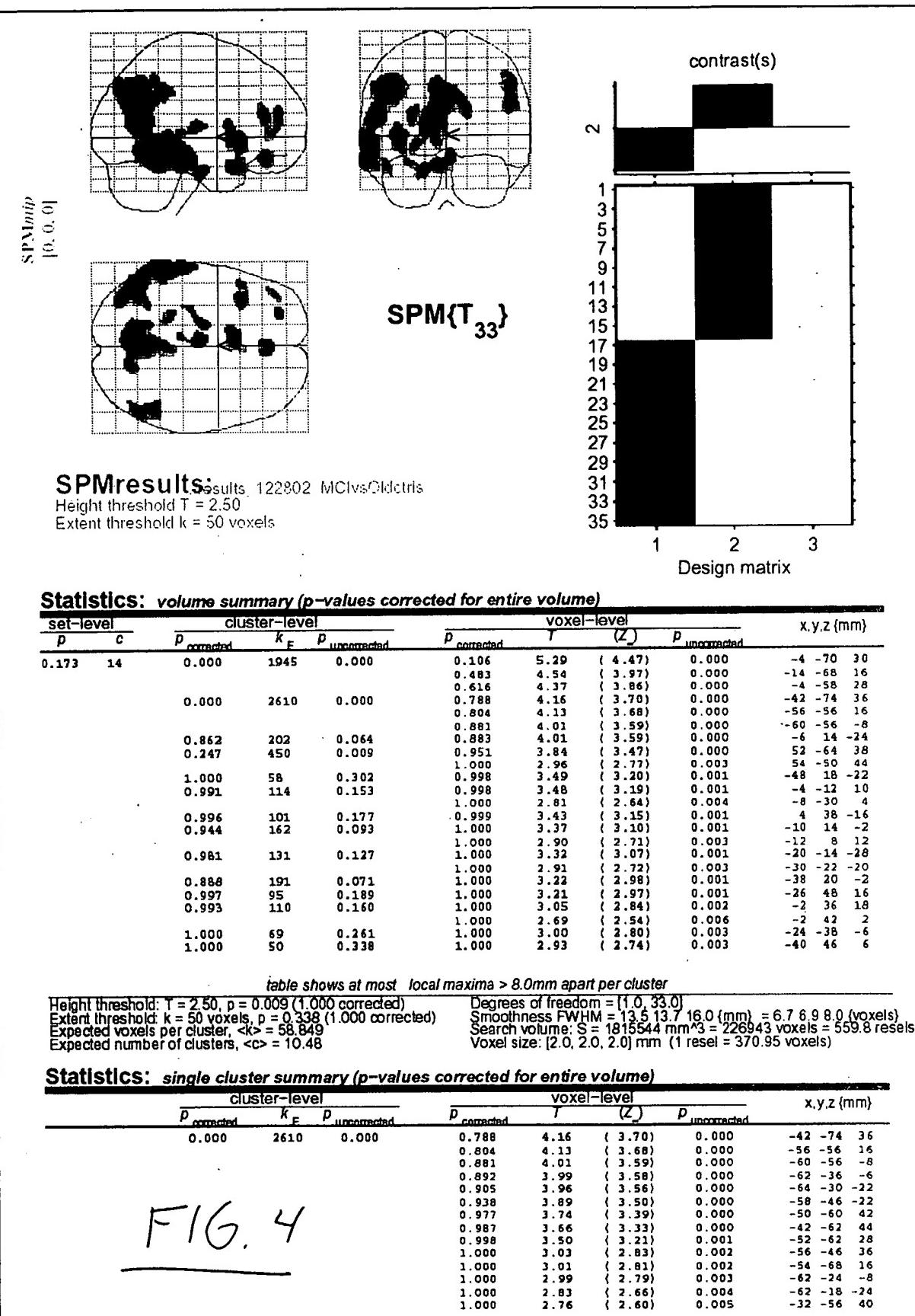
**FIG. 2b (Cont'd) Derivation of Region Location and Identification of VOIs**

- 500 CDI is Compared to Established Normal Range of Values; Presence of Normality or Abnormality is Determined
- 510 If CDI Reading is Negative, Patient Educated About the Clinical Course of Potential Illnesses and Signs to Watch out for; Potential Benefit of Preventative Measures such as Antioxidants, Brain Exercises, Beneficial Diet and Adequate Rest are Discussed
- 520 If CDI Reading is Positive, Patient Educated about the Meaning of a Positive CDI Reading, Projected Clinical Course of Illness, Benefit of Medication, Potential Benefit of Preventative Measures such as Antioxidants, Brain Exercises, Beneficial Diet and Adequate Rest are Discussed
- 530 Following either Step 620 or Step 630, Results are Given to Referring Physician and Patient Scheduled for Re-evaluation in one year.
- 540 Patient Data is Stored in the Comprehensive Patient Database

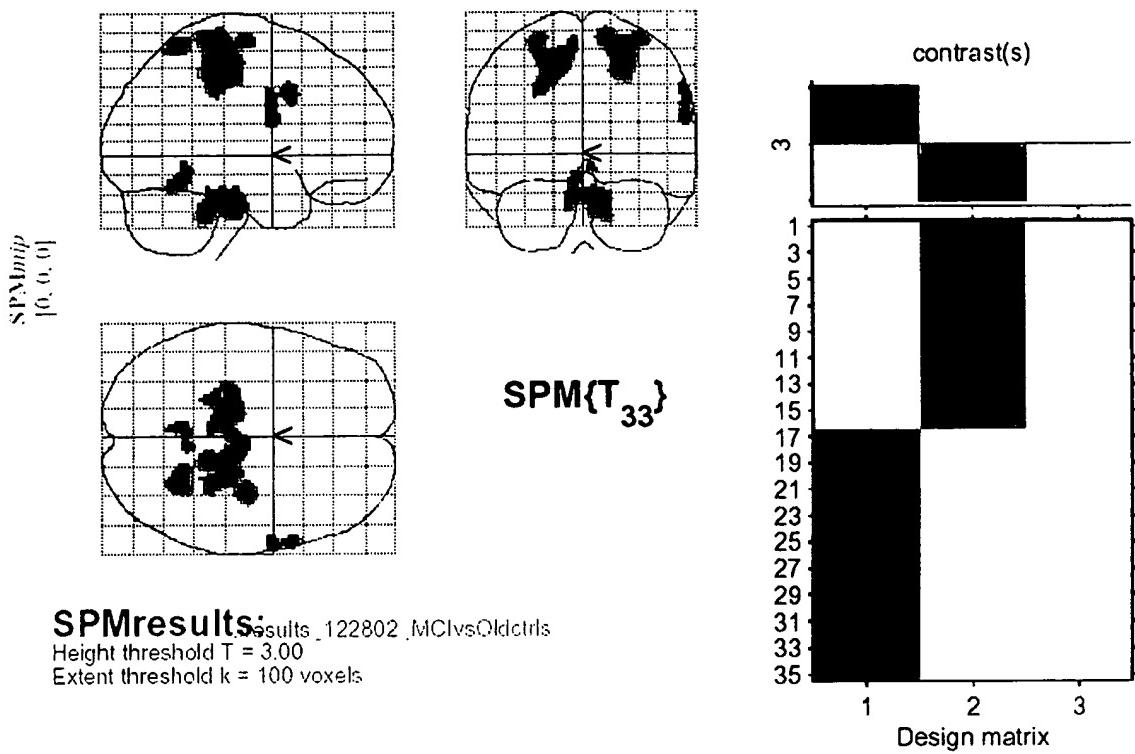
**FIG. 2c      Patient Diagnosis and Clinical Recommendations**



**Fig. 3**



## Increases in MCI



**Statistics: volume summary (p-values corrected for entire volume)**

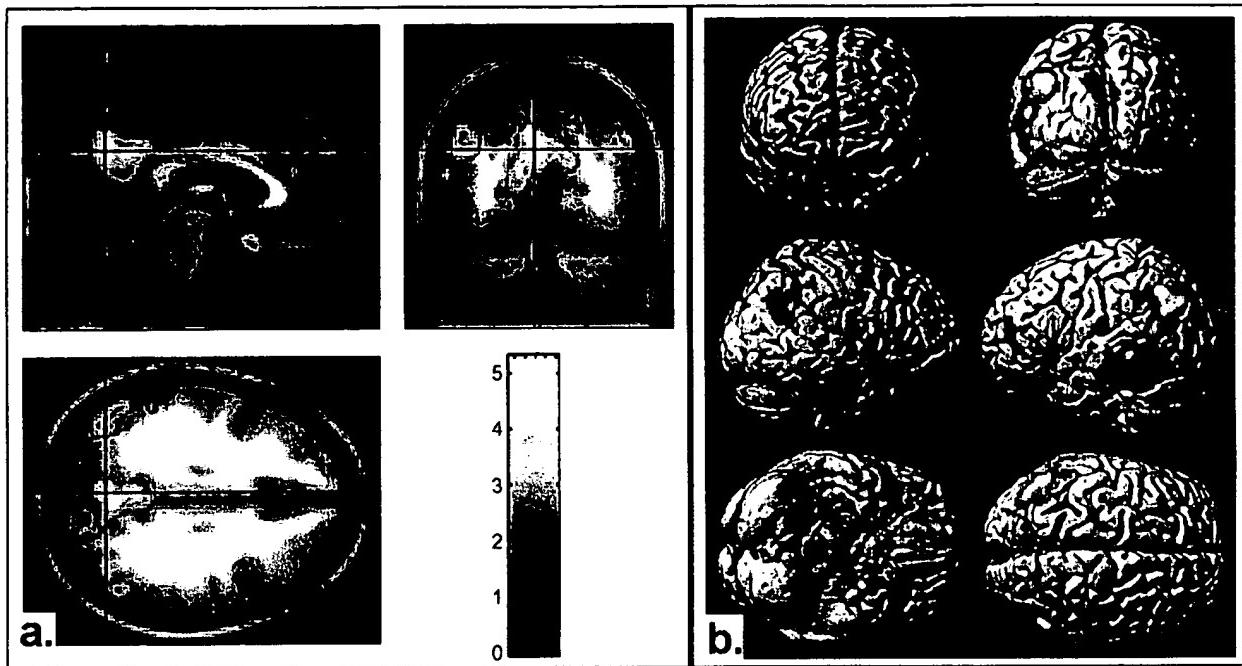
set-level		cluster-level		voxel-level			x,y,z (mm)	
p	c	p <sub>corrected</sub>	k <sub>E</sub>	p <sub>uncorrected</sub>	p <sub>corrected</sub>	T	(Z)	p <sub>uncorrected</sub>
0.003	6	0.002	745	0.000	0.027	5.86 (-4.82)	0.000	-16 -24 52
				0.528	4.48 (-3.93)	0.000	-26 -26 66	
				0.773	4.18 (-3.71)	0.000	-6 -34 62	
		0.318	188	0.026	0.120	5.23 (-4.43)	0.000	26 -54 64
		0.003	678	0.000	0.202	5.00 (-4.28)	0.000	10 -22 -30
				0.622	4.37 (-3.85)	0.000	14 -38 -34	
				0.925	3.92 (-3.52)	0.000	-6 -28 -24	
		0.001	873	0.000	0.379	4.68 (-4.07)	0.000	34 -16 68
				0.434	4.60 (-4.02)	0.000	26 -32 52	
				0.596	4.40 (-3.87)	0.000	14 -38 68	
		0.530	138	0.051	0.837	4.08 (-3.65)	0.000	62 12 36
				0.937	3.89 (-3.50)	0.000	62 0 22	
				0.994	3.59 (-3.28)	0.001	62 0 34	
		0.683	110	0.077	0.995	3.57 (-3.26)	0.001	-6 -54 -16
				1.000	3.30 (-3.05)	0.001	4 -50 -6	

table shows at most local maxima > 8.0mm apart per cluster

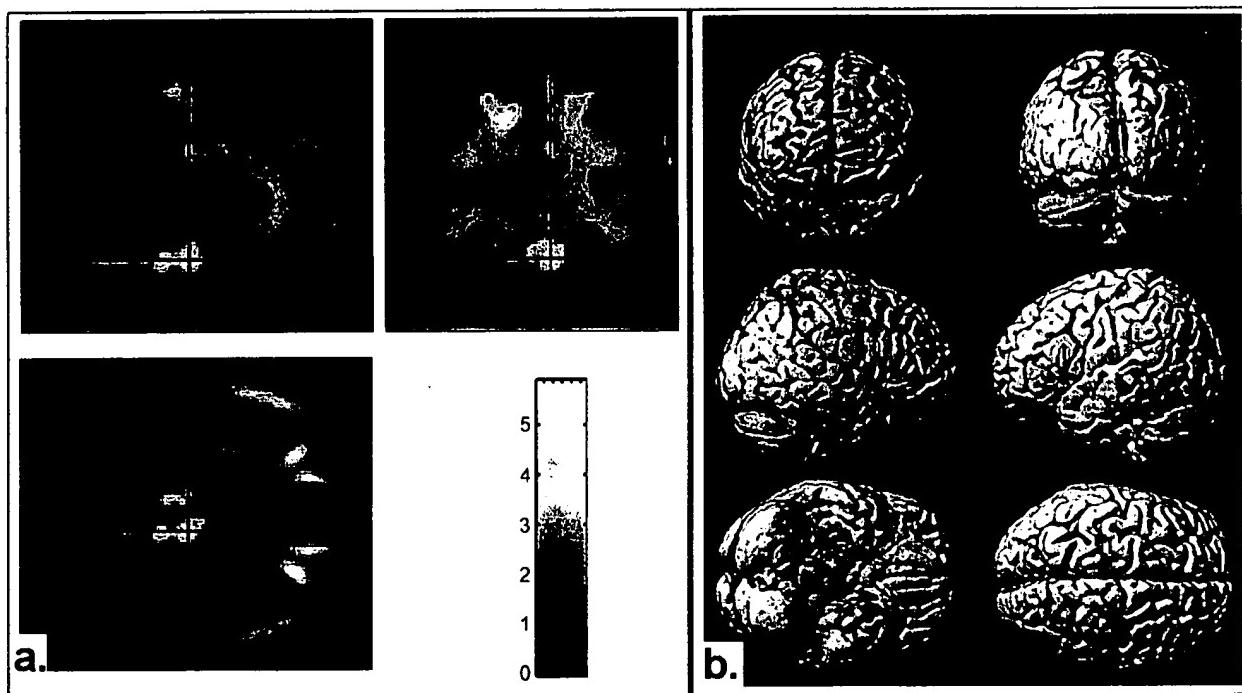
Height threshold: T = 3.00, p = 0.003 (1.000 corrected)  
 Extent threshold: k = 100 voxels, p = 0.090 (0.739 corrected)  
 Expected voxels per cluster,  $\langle k \rangle = 35.683$   
 Expected number of clusters,  $\langle c \rangle = 1.34$

Degrees of freedom = [1, 0, 33, 0]  
 Smoothness FWHM = 13.5 13.7 16.0 {mm} = 6.7 6.9 8.0 {voxels}  
 Search volume: S = 1815544 mm<sup>3</sup> = 226943 voxels = 559.8 resels  
 Voxel size: [2.0, 2.0, 2.0] mm (1 resel = 370.95 voxels)

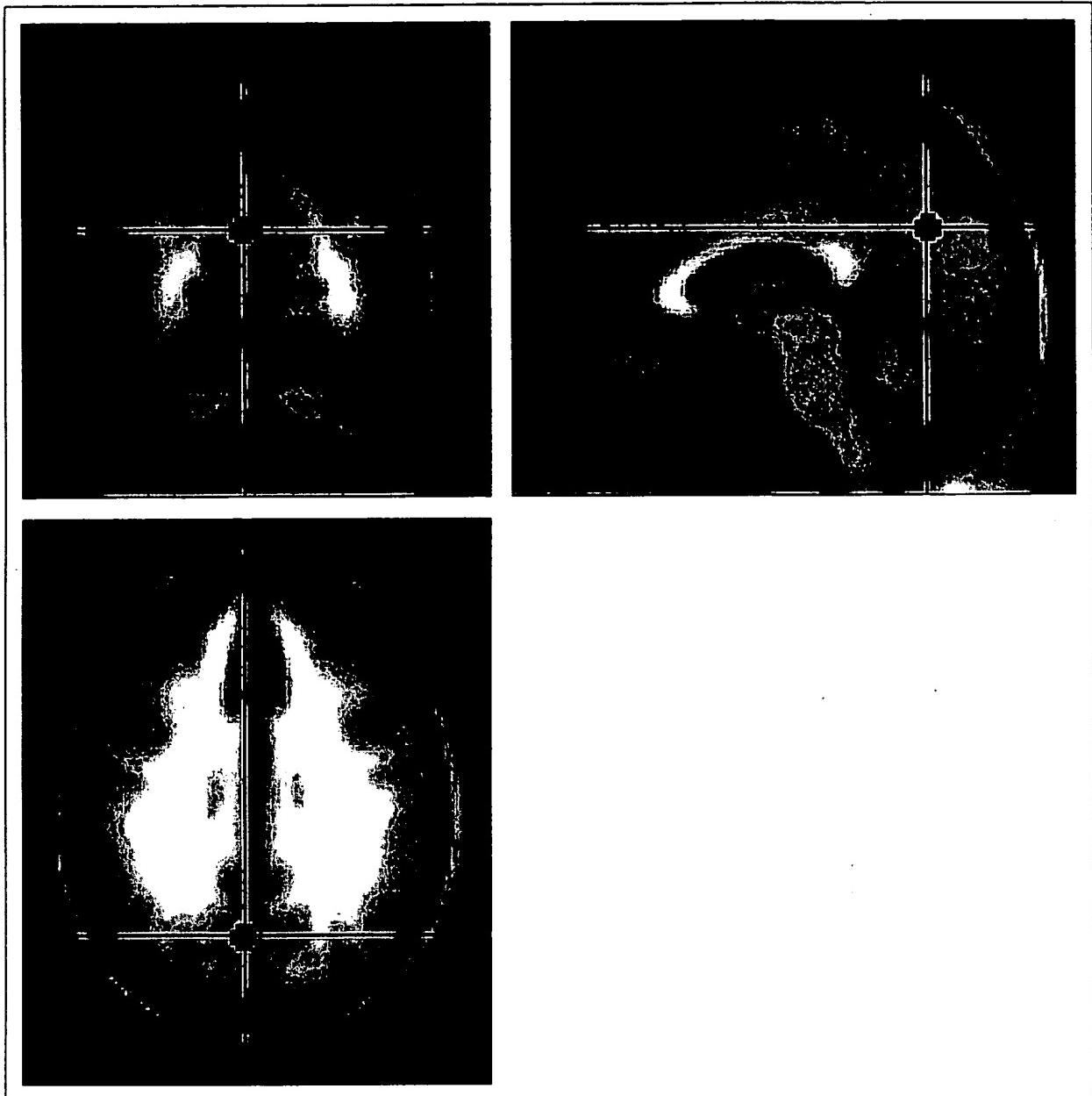
**Fig. 5**



**Fig. 6**



**Fig. 7**



**Fig. 8**

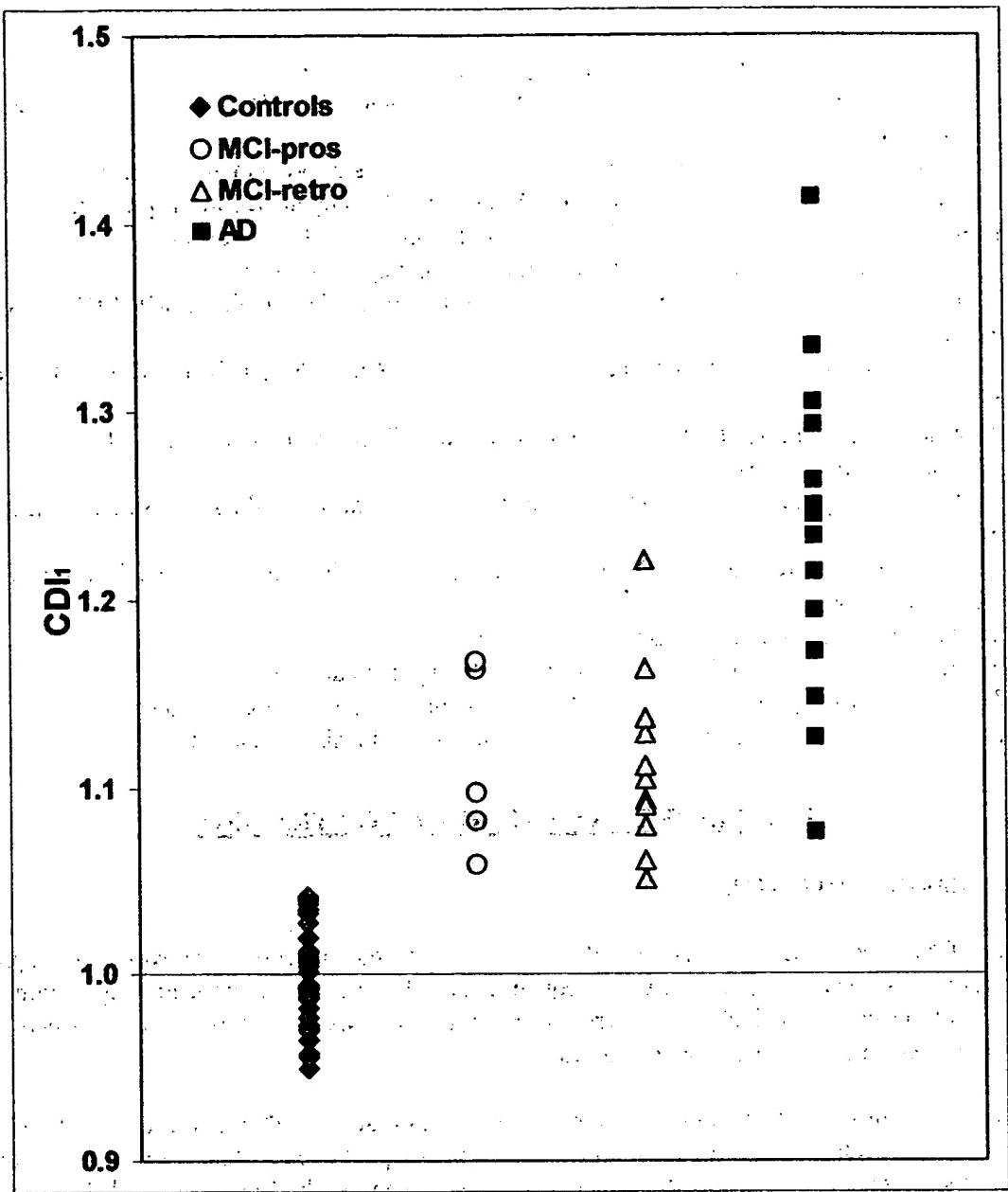


FIG. 9

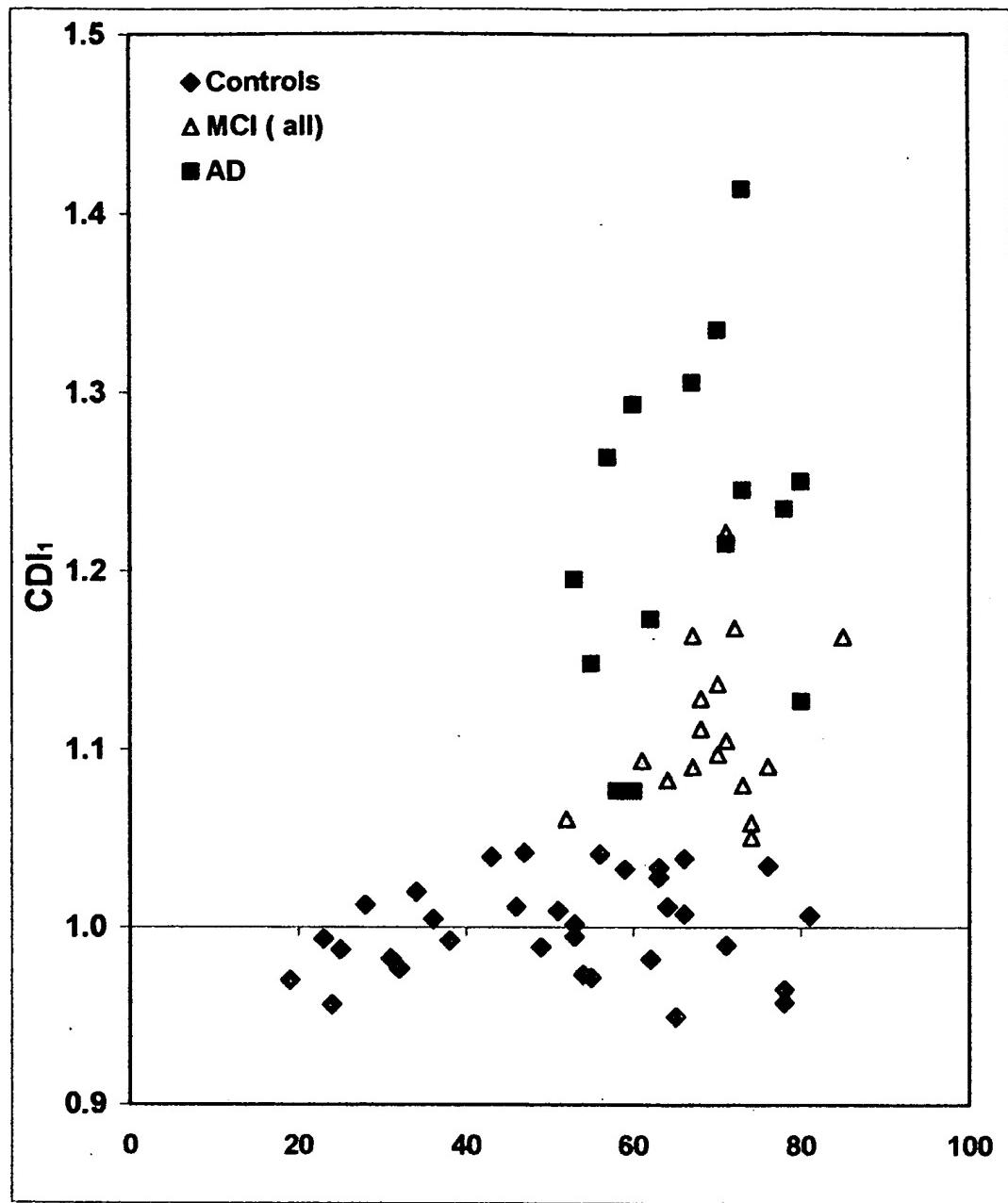


FIG. 10

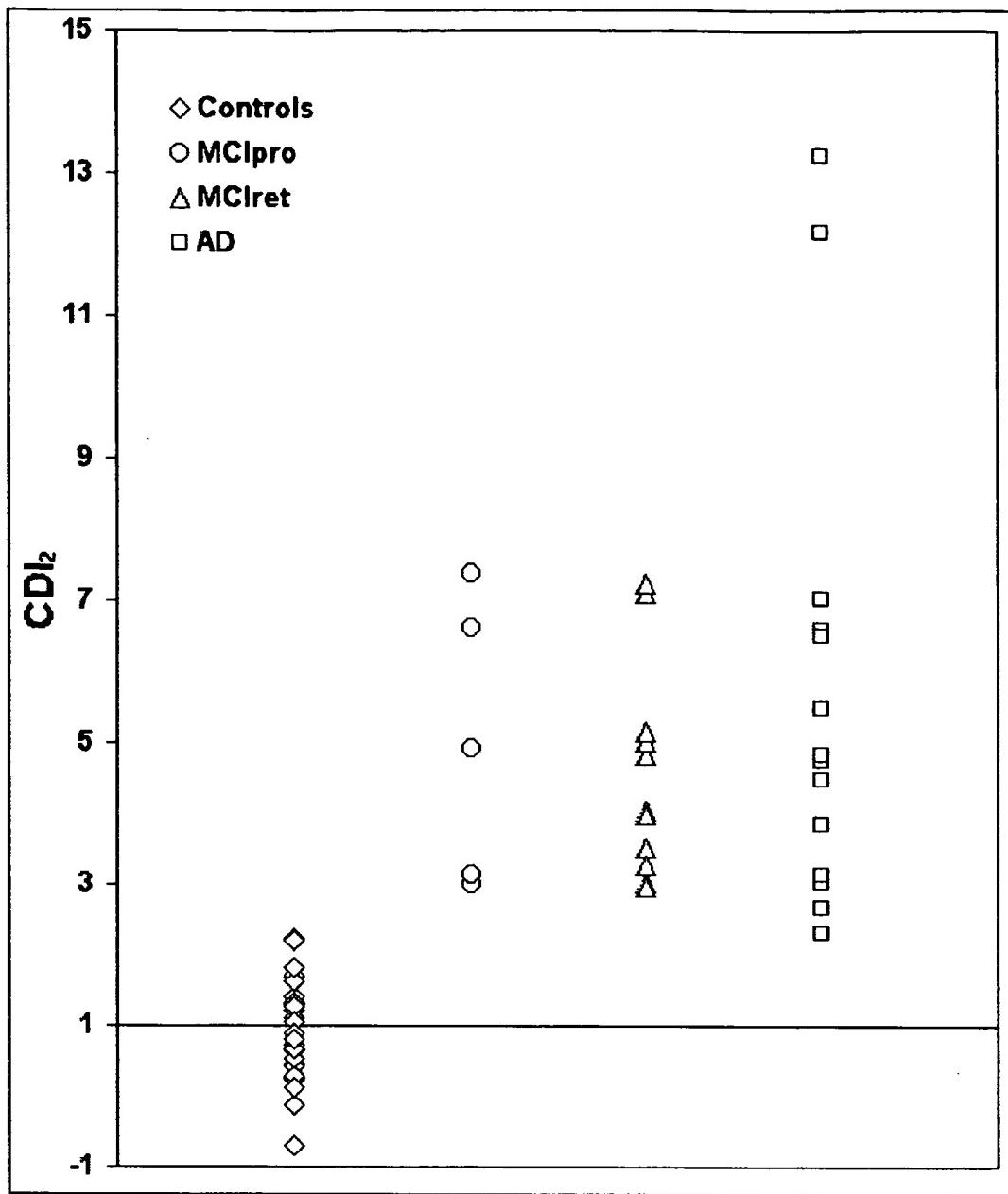
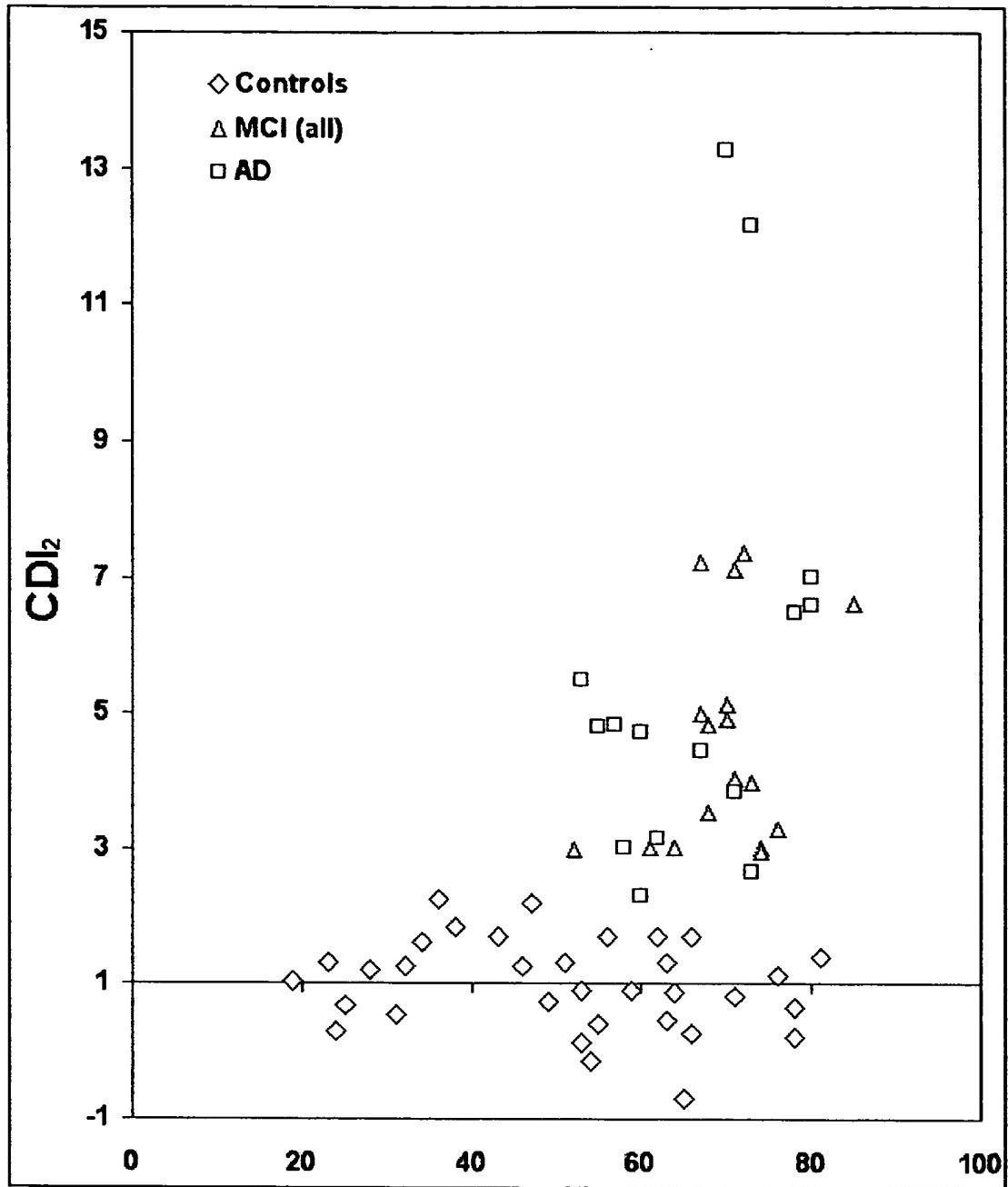


FIG. 11



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